

This listing of claims will replace all prior versions, and listings, of claims in the application:

**LISTING OF CLAIMS:**

Claim 1 (canceled)

Claim 2 (amended): ~~An~~ The isolated nucleic acid molecule encoding a replication competent recombinant Hepatitis C Virus (HCV) genome ~~of claim 1~~, which nucleic acid comprises from 5' to 3' on the positive-sense nucleic acid

(a) a functional 5' HCV non-translated region (NTR) comprising an extreme 5'-terminal conserved sequence;

(b) at least one open reading frame (ORF) encoding a heterologous gene operatively associated with an expression control sequence, wherein the heterologous gene and expression control sequence are oriented on the positive-strand nucleic acid molecule;

(c) an ORF encoding at least a portion of an HCV polyprotein whose cleavage products form functional components of HCV virus particles and RNA replication machinery, and

(d) an HCV 3' NTR comprising an extreme 3'-terminal conserved sequence, and wherein said nucleic acid contains at least one mutation in the HCV sequence and is able to replicate efficiently when transfected into a susceptible cell line without reducing the growth rate of said cell line by more than 10 fold.

Claim 3 (amended): The isolated nucleic acid of ~~claim 1~~ claim 2, wherein the susceptible cell line is selected from the group consisting of human hepatoma cell line Huh-7, human hepatoma cell line HepG2, hepatoma cell line PH5CH, *T. belangeri* liver cell line MBTL, human diploid fibroblast cell line VERO, secondary monkey kidney cell line CV-1, T cell line MT-2, T cell line HPBMa10-2, T cell line MOLT-4, and B cell line Daudi.

Claim 4 (amended, withdrawn): The isolated nucleic acid of claim 2, wherein the susceptible cell line of ~~claim 4~~, which is human hepatoma cell line Huh-7.

Claim 5 (amended): The isolated nucleic acid molecule according to ~~claim 1~~ claim 2, which is selected from the group consisting of double stranded DNA, single stranded DNA, double stranded RNA, and single stranded RNA.

Claim 6 (amended, withdrawn): The ~~An~~ isolated nucleic acid molecule of claim 2, which is not more than 99.9% identical and is at least 95% identical to SEQ ID NO: 1.

Claim 7 (original, withdrawn): The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of HCVR 2 (SEQ ID NO: 2).

Claim 8 (original, withdrawn): The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of HCVR 8 (SEQ ID NO: 3).

Claim 9 (original, withdrawn): The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of HCVR 9 (SEQ ID NO: 4).

Claim 10 (original, withdrawn): The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of HCVR 22 (SEQ ID NO: 5).

Claim 11 (original, withdrawn): The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of HCVR 24 (SEQ ID NO: 6).

Claim 12 (amended, withdrawn): A stable cell line transfected with the isolated nucleic acid molecule according to ~~claim 1~~ claim 2, wherein said cell line:

(e) has a growth rate which is not less than 10% of the growth rate of the corresponding naïve cell line, and

(f) is capable of supporting efficient replication of said isolated nucleic acid.

Claim 13 (original, withdrawn): The cell line of claim 12 wherein said cell line is selected from the group consisting of human hepatoma cell line Huh-7, human hepatoma cell line HepG2, hepatoma cell line PH5CH, *T. belangeri* liver cell line MBTL, human diploid fibroblast cell line VERO, secondary monkey kidney cell line CV-1, T cell line MT-2, T cell line HPBMa10-2, T cell line MOLT-4, and B cell line Daudi.

Claim 14 (original, withdrawn): The cell line of claim 12 wherein said cell line is derived from a human hepatoma cell line Huh-7.

Claim 15 (original, withdrawn): The cell line of claim 14 designated HCVR 2 and having ATCC Accession No. PTA-2489.

Claim 16 (original, withdrawn): The cell line of claim 14 designated HCVR 8 and having ATCC Accession No. PTA-2490.

Claim 17 (original, withdrawn): The cell line of claim 14 designated HCVR 9 and having ATCC Accession No. PTA-2486.

Claim 18 (original, withdrawn): The cell line of claim 14 designated HCVR 22 and having ATCC Accession No. PTA-2487.

Claim 19 (original, withdrawn): The cell line of claim 14 designated HCVR 24 and having ATCC Accession No. PTA-2488.

Claim 20 (withdrawn): A method of screening for anti-HCV therapeutics, which method comprises comparing a level of HCV subgenomic replicon RNA or replicon RNA-associated protein expression in the cell line of claim 12 contacted with a candidate therapeutic agent to the cell line not contacted with the candidate therapeutic agent, wherein a decrease in the level of HCV subgenomic replicon RNA or replicon RNA-associated protein expression is indicative of the inhibitory activity of the agent.

Claim 21 (withdrawn): A method for detecting antibodies to HCV in a biological sample from a subject comprising contacting said sample with the protein fractions derived from the cell line of claim 12 under conditions that permit interaction of HCV-specific antibodies in the sample with the HCV protein(s) produced in said cell line, followed by detecting binding of the antibodies in the sample to these HCV-derived protein(s), wherein said binding is indicative of the presence of HCV infection in the subject from which the sample was derived.

Claim 22 (withdrawn): The method of claim 21 wherein said biological sample is selected from the group consisting of blood, serum, plasma, blood cells, lymphocytes, and liver cells.